

Appl. No. : 09/344,526  
Filed : June 24, 1999

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

#### LISTING OF CLAIMS

- 1-15. (Cancelled)
16. (Currently amended) A method of making a bead ~~microsphere~~ array comprising:
- a) contacting a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm<sup>2</sup>, with a solution comprising a population of different beads ~~particles~~, wherein said beads ~~particles~~ do not comprise an optical signature; and
  - b) applying energy to said substrate or said solution, or both, such that at least a subpopulation of said different beads ~~particles~~ randomly associate onto sites.
17. (Original) A method according to claim 16 wherein said discrete sites comprise wells.
18. (Original) A method according to claim 16 wherein said energy is in the form of agitation.
19. (Currently amended) A method according to claim 16, wherein said energy is dipping said substrate into said beads ~~particles~~.
20. (Previously presented) A method according to claim 19, wherein said substrate is a fiber optic bundle.
- 21-58. (Cancelled)
59. (Previously presented) A method of determining the presence of a target analyte in a sample comprising:
- a) contacting said sample with an array comprising:
    - i) substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm<sup>2</sup>, wherein said sites are wells; and
    - ii) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising:

(a) a different bioactive agent; and

(b) a different identifier binding ligand;

b) determining the presence or absence of said target analyte; and

c) decoding a location of said bioactive agent by correlating said bioactive agent with said location, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to a first and second identifier binding ligands, whereby said first and second identifier binding ligands identify said first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

60. (Previously presented) The method according to claim 59, wherein said first and second bioactive agents comprise nucleic acids.

61. (Previously presented) The method according to claim 60, wherein said nucleic acids comprise DNA.

62. (Previously presented) The method according to claim 60, wherein said nucleic acids comprise single stranded nucleic acids.

63. (Previously presented) The method according to claim 60, wherein said nucleic acids comprise double stranded nucleic acids.

64. (Previously presented) The method according to claim 59, wherein said first and second bioactive agents comprise proteins.

65. (Previously presented) The method according to claim 59, wherein said substrate comprises a fiber optic bundle.

66-74. (Cancelled)

75. (Currently amended) The method according to claim 16, wherein said population of different beads ~~particles~~ comprises at least a first and second subpopulation.

76. (Previously presented) The method according to claim 75, wherein said first and second subpopulations each comprise a different bioactive agent.

77. (Previously presented) The method according to claim 76, wherein said bioactive agent comprises a protein.

78. (Previously presented) The method according to claim 76, wherein said bioactive agent comprises a nucleic acid.

79. (Previously presented) The method according to claim 78, wherein said nucleic acid comprises DNA.

80. (Currently amended) The method according to claim 76, wherein said first and second subpopulations of beads ~~partieles~~ each comprise a different identifier binding ligand.

81. (Previously presented) The method according to claim 80, wherein said identifier binding ligand comprises a protein.

82. (Previously presented) The method according to claim 80, wherein said identifier binding ligand comprises a nucleic acid.

83. (Previously presented) The method according to claim 82, wherein said bioactive agent and said identifier binding ligand within the same subpopulation each comprise an identical nucleic acid sequence for binding a decoder binding ligand.

84. (Previously presented) The method according to claim 80 further comprising decoding a location of said bioactive agent on said array by correlating said bioactive agent with said location, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to first and second identifier binding ligands, whereby said first and second identifier binding ligands identify said first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

85. (Previously presented) The method according to claim 84, wherein said decoder binding ligands comprise proteins.

86. (Previously presented) The method according to claim 84, wherein said decoder binding ligands comprise nucleic acids.

87. (Previously presented) The method according to claim 16, wherein said substrate comprises a flat planar substrate.

88. (Previously presented) The method according to claim 59, wherein said identifier binding ligands comprise proteins.

89. (Previously presented) The method according to claim 59, wherein said identifier binding ligands comprise nucleic acids.

90. (Previously presented) The method according to claim 59, wherein comprise decoder binding ligands are proteins.

91. (Previously presented) The method according to claim 59, wherein comprise decoder binding ligands are nucleic acids.

92. (Previously presented) The method according to claim 59, wherein said substrate comprises a flat planar substrate.

93. (Currently amended) A method of determining the presence of a target analyte in a sample comprising:

a) contacting said sample with an array comprising:

i) a substrate with a surface comprising sites at a density of at least 100 sites per 1 mm<sup>2</sup>, wherein said sites are present in a depression; and

ii) a population of particles randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising:

(a) a different bioactive agent; and

(b) a different identifier binding ligand;

b) decoding a location of said bioactive agent by correlating said bioactive agent with said location, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to a first and second identifier binding ligands, whereby said first and second identifier binding ligands identify said first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array; and

c) determining the presence or absence of said target analyte.

94. (Previously presented) The method according to claim 93, wherein said bioactive agents comprise nucleic acids.

95. (Previously presented) The method according to claim 94, wherein said nucleic acids comprise DNA.

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96. (Previously presented) The method according to claim 94, wherein said nucleic acids comprise single stranded nucleic acids.

97. (Previously presented) The method according to claim 94, wherein said nucleic acids comprise double stranded nucleic acids.

98. (Previously presented) The method according to claim 93, wherein said bioactive agents comprise proteins.

99. (Previously presented) The method according to claim 93, wherein said identifier binding ligands comprise proteins.

100. (Previously presented) The method according to claim 93, wherein said identifier binding ligands comprise nucleic acids.

101. (Previously presented) The method according to claim 93, wherein said decoder binding ligands comprise proteins.

102. (Previously presented) The method according to claim 93, wherein said decoder binding ligands comprise nucleic acids.

103. (Previously presented) The method according to claim 93, wherein said substrate comprises a fiber optic bundle.

104. (Previously presented) The method according to claim 93, wherein said substrate comprises a flat planar substrate.

105. (Previously presented) The method according to claim 93, wherein said particles are beads.

106. (Canceled)

107. (Canceled)

108. (Currently amended) The method according to claim 93 ~~107~~, wherein said sites are contiguous.

109. (New) A method of determining the presence of a target analyte in a sample comprising:

a) contacting said sample with an array comprising:

i) a substrate with a surface comprising sites at a density of at least 100 sites per 1 mm<sup>2</sup>, wherein said sites comprise wells; and

ii) a population of particles randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising:

- (a) a different bioactive agent; and
- (b) a different identifier binding ligand;

b) decoding a location of said bioactive agent by correlating said bioactive agent with said location, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to a first and second identifier binding ligands, whereby said first and second identifier binding ligands identify said first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array; and

c) determining the presence or absence of said target analyte.

110. (New) The method according to claim 109, wherein said sites are discrete sites.

111. (New) The method according to claim 109, wherein said bioactive agents comprise nucleic acids.

112. (New) The method according to claim 111, wherein said nucleic acids comprise DNA.

113. (New) The method according to claim 111, wherein said nucleic acids comprise single stranded nucleic acids.

114. (New) The method according to claim 111, wherein said nucleic acids comprise double stranded nucleic acids.

115. (New) The method according to claim 109, wherein said bioactive agents comprise proteins.

116. (New) The method according to claim 109, wherein said identifier binding ligands comprise proteins.

117. (New) The method according to claim 109, wherein said identifier binding ligands comprise nucleic acids.

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118. (New) The method according to claim 109, wherein said decoder binding ligands comprise proteins.

119. (New) The method according to claim 109, wherein said decoder binding ligands comprise nucleic acids.

120. (New) The method according to claim 109, wherein said substrate comprises a fiber optic bundle.

121. (New) The method according to claim 109, wherein said substrate comprises a flat planar substrate.

122. (New) The method according to claim 109, wherein said particles are beads.

123. (New) A method of making a particle array comprising:

a) contacting a substrate with a surface comprising sites at a density of at least 100 sites per 1 mm<sup>2</sup>, with a solution comprising a population of different particles, wherein said particles do not comprise an optical signature, and wherein said sites comprise wells; and

b) applying energy to said substrate or said solution, or both, such that at least a subpopulation of said different particles randomly associate onto sites.

124. (New) The method according to claim 123, wherein said sites are discrete sites.

125. (New) The method according to claim 123, wherein said energy is in the form of agitation.

126. (New) The method according to claim 123, wherein said energy is dipping said substrate into said particles.

127. (New) The method according to claim 123, wherein said substrate is a fiber optic bundle.

128. (New) The method according to claim 123, wherein said population of different particles comprises at least a first and second subpopulation.

129. (New) The method according to claim 128, wherein said first and second subpopulations each comprise a different bioactive agent.

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130. (New) The method according to claim 129, wherein said bioactive agent comprises a protein.

131. (New) The method according to claim 129, wherein said bioactive agent comprises a nucleic acid.

132. (New) The method according to claim 131, wherein said nucleic acid comprises DNA.

133. (New) The method according to claim 129, wherein said first and second subpopulations of particles each comprise a different identifier binding ligand.

134. (New) The method according to claim 133, wherein said identifier binding ligand comprises a protein.

135. (New) The method according to claim 133, wherein said identifier binding ligand comprises a nucleic acid.

136. (New) The method according to claim 135, wherein said bioactive agent and said identifier binding ligand within the same subpopulation each comprise an identical nucleic acid sequence for binding a decoder binding ligand.

137. (New) The method according to claim 133 further comprising decoding a location of said bioactive agent on said array by correlating said bioactive agent with said location, whereby said decoding comprises contacting said array with at least first and second different decoder binding ligands, whereby said first and second decoder binding ligands bind to first and second identifier binding ligands, whereby said first and second identifier binding ligands identify said first and second bioactive agents, respectively, to thereby identify a location of said first and second bioactive agents to thereby decode said array.

138. (New) The method according to claim 137, wherein said decoder binding ligands comprise proteins.

139. (New) The method according to claim 137, wherein said decoder binding ligands comprise nucleic acids.

140. (New) The method according to claim 123, wherein said substrate comprises a flat planar substrate.



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## **SUMMARY OF INTERVIEW**

### Identification of Claims Discussed

Claim 59-65 and 88-92 were discussed.

### Identification of Prior Art Discussed

U.S. Patent No. 5,326,691

### Proposed Amendments

Discussed possible alternatives to the term "particle."

### Principal Arguments and Other Matters

Discussed allowability of claims 59-65 and 88-92.

### Results of Interview

The Examiner agreed to recast Office Action mailed June 15, 2005 so as to indicate the allowability of claims 59-65 and 88-92.